An atypical location for Malignant Triton Tumor – a case report

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Abstract: The authors report a case of a 52-years-old female patient, without personal or family history of genetic diseases, referred to our institution after an atypical gastrectomy with R2 resection for a gastric tumor suspected to be a GIST. Histopathological review was performed and a diagnosis of a high-grade mesenchymal malignant neoplasm with rhabdomyoblastic heterologous differentiation, compatible with malignant Triton tumor, was rendered. After excluding residual disease, the patient was proposed to adjuvant chemotherapy. Two months later, a follow-up CT-scan showed a local recurrence, with no metastatic spread. After multidisciplinary team decision, she was submitted to R0 resection of the tumor consisting in total gastrectomy and splenectomy. Histopathological examination confirmed the recurrence of malignant Triton tumor of gastric wall, with free margins. The patient was proposed for surveillance and currently there is no evidence of recurrent disease after 18-months.

Keywords: Malignant Triton tumor; Malignant peripheral nerve sheath tumor; Sarcoma; Soft tissue tumor; Stomach.

1. Introduction

Soft tissue neoplasms or sarcomas are rare tumors, with an incidence of approximately 5 cases per 100,000 inhabitants per year and are comprised of approximately 70 subtypes. Each of these subtypes is characterized by distinct morphological features, leading to a specific clinical behavior and, consequently, requiring a tailored therapeutic approach [1]. Malignant Peripheral Nerve Sheath Tumors (MPNST) represent about 5-10% of all soft tissue sarcomas. Malignant Triton Tumor (MTT) arises from divergent rhabdomyoblastic differentiation within MPNST and can occur in approximately 15% of the latter [2]. Despite the rarity, MTT is associated with a worse outcome than MPNST [4], marked by early relapses and short survival expectancy, with a 5-year survival rate of 10% [5, 6].

MTT is traditionally associated with type-1 neurofibromatosis (NF1) or von Recklingausen’s disease [3,6] but it can occur in individuals without genetic susceptibility syndromes [7]. Sporadic MTT exhibit a female predominance and is typically diagnosed in the fifth decade of life [4]. The most common tumor locations include the head and neck, trunk and extremities, while intra-abdominal MTTs are rare, with only a few reported cases [4, 8, 9]. The primary challenge in managing MTT lies in its diagnosis. Given the histopathological overlap between MTT, MPNST, and other diagnostic entities, along with the intratumoral heterogeneity of these neoplasms and variations in the definition of rhabdomyoblastic heterologous differentiation, well defined criteria for the diagnosis of
MTT are currently a matter of debate and study [2]. In addition, given its rarity, the available evidence for the treatment of this tumor is limited with only small case series reported. Nevertheless, similar to MPNST, surgery with negative margins is the standard treatment for resectable MTT, complemented by adjuvant radiotherapy and chemotherapy [6,10]. Due to the rarity, complexity and heterogeneity of the MTT, as well as all sarcoma subtypes, the management of such neoplasms should be centralized in expert centers.

2. Case Report

The authors report a case of a 52-years-old female patient, healthy, without personal or family diagnosis of NF1 or other genetic susceptibility syndromes. This patient presented symptomatic anemia in February 2021, requiring blood transfusion and significant weight loss. She underwent an endoscopic study that revealed a submucosal tumor with central ulceration in the gastric fundus, suspected to be a gastrointestinal stromal tumor (GIST). Fine needle aspiration biopsy was performed but it was inconclusive. A CT scan showed an expansive lesion measuring 59x57mm in the gastric fundus and no evidence of distant metastasis.

Due to the suspicion of a GIST, the patient underwent exploratory laparotomy in March 2021, in a general hospital, which disclosed a large proximal gastric endophytic neoplasm without involvement of the serosa, located at the lesser curvature approximately 1-2cm from the gastroesophageal junction. An atypical gastrectomy for resection was performed, but accidentally rupture of the tumor occurred during dissection. The postoperative period was uneventful, and the patient was discharged on the 6th postoperative day. Histopathological evaluation showed a high grade mesenchymal malignant neoplasm of the gastric wall. Immunohistochemistry was positive for desmin and myogenin, and negative for CD117, DOG1 and S100 protein, and a diagnosis of pleomorphic rhabdomyosarcoma was rendered.

After this result, the patient was referred to our institution, a specialized sarcoma hospital. Histopathological review of paraffin blocks was performed by an expert pathologist in soft tissue tumors using a wider immunohistochemical panel and genetic studies. Histological analysis showed a malignant mesenchymal neoplasm, with variable cellularity and morphology, predominantly composed of oval-shaped cells with moderate cytoplasm, vesicular nuclei and prominent nucleoli, organized in fascicles with a herringbone pattern. Numerous cells with rhabdoid features (eosinophilic cytoplasm and eccentric nuclei) and some multinucleated giant cells were also observed. The mitotic index exceeded 20 mitoses per 10 high-power fields. The tumor cells showed multifocal positivity for desmin, focal positivity for MyoD1 and myogenin, negativity for S100 protein and complete loss of expression of H3K27me3 (Figure 1).

Figure 1: Histological examination of malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation (Malignant Triton tumor). A. Hematoxylin-Eosin, original magnification x10. B. Loss of expression of H3K27me3, original magnification x10. C. Positive immunoreactivity for myogenin in the rhabdomyoblastic-like cells, original magnification x10.
These findings supported the diagnosis of MPNST with heterologous rhabdomyoblastic differentiation or MTT. Genetic analysis of the tumor was also performed, revealing a pathogenic variant on the NF1 gene, which supports the diagnosis. PET-scan in June 2021 showed no evidence of residual disease. The patient was proposed for adjuvant chemotherapy, due to tumor rupture on initial surgery and completed six cycles of doxorubicin between July and November 2021. The first imaging evaluation after chemotherapy in January 2022 with CT scan revealed a local recurrence in the form of a solid and heterogeneous mass measuring 5cm in the left hypochondrium, originated from the wall of the greater curvature of the stomach, with no evidence of lymph node or distant metastasis (Figure 2 and 3).

Figure 2: CT scan showing local recurrence of gastric Malignant Triton tumor – axial section.

Figure 3: CT scan showing local recurrence of gastric Malignant Triton tumor – coronal section.
The Multidisciplinary Tumor Board decided on surgical resection. In March 2022, the patient underwent surgery, which revealed a 12 cm mass originating from the gastric greater curvature in the left hypochondrium, with the involvement of splenic hilum and adherences to left diaphragm peritoneum. Extensive resection was performed, including total gastrectomy and en-bloc splenectomy. Roux-en-Y antecolic esophagojejunostomy reconstruction was undertaken. The procedure was uneventful, and the patient was discharged home at 8th day postoperative without any complication.

Histology confirmed the persistence/recurrence of the previously evaluated neoplasm with focal infiltration of the outer half of the muscularis propria, negative margins, and no metastasized lymph nodes. The patient was proposed for surveillance through a comprehensive clinical and imaging assessment, including thoracoabdominal-pelvic CT scans every 3 months during the initial three years, with subsequent follow-ups spaced at extended intervals thereafter. The patient had undergone a full recovery from surgery and there is no evidence of recurrent disease after eighteen months of the surgery.

3. Discussion and conclusion

Herein the authors present a sporadic case of MTT of the gastric wall in a female patient, an unusual location for this tumor. This patient initially underwent preoperative diagnostic evaluation and surgery at a non-specialized sarcoma hospital and was referred to our expert center only after the histopathological diagnosis of a high-grade sarcoma. At present is strongly recommended that management of sarcomas be conducted at a specialized center as early as possible, due to specific diagnostic studies and treatment strategies, which are complex and distinct from other tumor types [10-13].

Presently, centralization of sarcomas in a specialized center is associated with a more accurate preoperative diagnosis, essential to plan a proper treatment [11, 12]. The histopathological diagnosis of MTT is particularly challenging due to its intratumoral heterogeneity and potential to mimic other tumor types such as spindle cell rhabdomyosarcoma, synovial sarcoma, among others, requiring the expertise of pathologists experienced in soft tissue tumors [2]. Beyond histomorphological assessment, immunohistochemistry using a broad panel marker is crucial for achieving a correct diagnosis [2].

In this case, preoperative fine needle aspiration biopsy proved inconclusive maybe because it was done using an immunohistochemistry panel specifically tailored for a diagnostic hypothesis of GIST. The absence of a preoperative diagnosis of a high-grade sarcoma, which could have anticipated a more intricate surgery, combined with the absence of a surgical team experienced in sarcoma procedures and attuned to the necessity of extended tumor resection, contributed to the inadvertent iatrogenic rupture of the tumor [18, 19]. Moreover, the initial histopathologic report suggesting a diagnosis of rhabdomyosarcoma was originated from a private laboratory using a restricted immunohistochemistry panel that failed to include the crucial marker, H3K27me3, essential for a diagnosis of MPNST and MTT [20]. In our institution the diagnosis of rhabdomyosarcoma was excluded despite positive staining for desmin, myogenin, and MyoD1, based on a complete loss of expression of H3K27me [14-16]. This marker played a pivotal role in the diagnosis of this case, as did the genetic testing for the NF1 gene, where pathologic variants are detected in 40% of MPNST cases [21]. It's noteworthy that both these analyses are more often available at expert sarcoma centers, underscoring the specialized nature of such diagnostic procedures.

In terms of surgical treatment, as it was mentioned before, it is recommended to entail an en bloc excision with negative margin [10] and should be performed at an expert center as it is associated with more R0 resections, less recurrence and increased survival [10-13]. On the other hand, tumor rupture is associated not only with local microscopic residual disease and local recurrence but also with systemic recurrence, as tumor cells can escape into the bloodstream, infiltrating distant organs [19]. Regularly, high-grade tumors with R1-R2 resections are proposed to adjuvant radiotherapy specially when re-excision is not feasible, thus enhancing local control in sarcomas [7, 10, 17]. Nevertheless, due to
the tumor’s specific location, radiotherapy entails a significant level of associated risk. In consideration of the risk of both local and systemic recurrence in this case, although there is no consistent data supporting the efficacy of adjuvant chemotherapy in MTT or MPNST [10,19], the Multidisciplinary Tumor Board proposed postoperative chemotherapy.

Despite the absence of systemic recurrence signs, an early relapsed was detected 9 months after the first surgery. In addition to the commonly observed associations between recurrence and large size coupled with high-grade histology [19], the likely pivotal factor for the early recurrence in this case appears to be the tumor rupture. Examining the local pattern of recurrence, as opposed to disseminated tumor foci, the authors posit that this particular case of recurrence is more closely linked to insufficient margins than to peritoneal contamination. Most likely this early relapsed or persistent disease was present as early as 3 months post-surgery but went undetected in the PET scan, given the imaging exam’s limitation in identifying lesions smaller than 1cm. Upon the early relapse, the surgical objective was to attain negative resection margins. Despite the challenge presented by centrally located tumors, which are often associated with reduced feasibility for obtaining negative margins [7], this was successfully accomplished through a complete resection en bloc with total gastrectomy and splenectomy. After the second surgery, the Multidisciplinary Tumor Board recommended surveillance due to the previous poor response to chemotherapy. This recommendation is also based on the understanding that the achieved adequate margin resection surgery is the only potentially curative treatment for soft tissue neoplasia.

In conclusion, this case highlights the importance of referral to a specialized sarcoma center to achieve a precise preoperative diagnosis of soft tissue neoplasms. That is pivotal in promoting a R0 resection at the initial surgery, as adequate margins continue to be the cornerstone of soft tissue neoplasm treatment, with chemotherapy typically falling short as a compensatory measure for suboptimal surgery. Even in cases of recurrence, surgical intervention remains a viable and successful option for resectable cases. In our case, obtaining an R0 resection has resulted in the absence of disease recurrence during the 18-month follow-up period. Furthermore, to the best of our knowledge, no malignant Triton tumor arising in the stomach has been published so far.

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References


